REMARKS

Status of Claims

Claims 1-9 and 12-95 are pending in the application. Claims 21-23, 32-34, 38-51, 65-67, 76-78 and 82-95 have been withdrawn from consideration. Claims 24, 35, 68 and 79 have been cancelled. Claims 1-9, 12-20, 24-31, 35-37, 52-64, 68-75 and 79-81 have been rejected. Claims 1, 31, 52, 59 and 69 have been amended.

Double Patenting Rejections

In the Office Action, the Examiner rejected claims 1-9, 12-20, 24-31, 35-37, 52-64, 68-75 and 79-81 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-85 of US 6,838,484 or over claims 1-10 of US 6,569,896 or over claims 1-5 of US 6,492,554. Applicants submit that the cited references are directed to O-bridged acyl-anilides which are not essentially identical in scope with the specifically claimed metabolites, and do not comprise overlapping claim scope. Applicants further request that allegations of double patenting be held in abeyance until such time as allowable claims are identified.

CLAIM REJECTIONS

35 U.S.C. § 103 Rejections

In the Office Action, the Examiner rejected claims 1-20, 24-31, 35-37, 52-64, 68-75 and 79-81 under 35 U.S.C. § 103(a), as allegedly being rendered obvious in view of the combined teaching of Tucker (US 4,636,505) and Miller et al (WO 98/55153). Applicants disagree.

Claims 1, 52, 69, and dependents therefrom, recite **metabolites** of the SARM compounds represented by formulas I, II, III, IV, VII, VIII, IX, X, which are hydroxylated, deacetylated or aminated derivatives of the O-Bridged SARM compounds, and possess anabolic and androgenic activity. Applicants submit that the metabolism of O-bridged compounds are substantially different from S-bridged compound (such as bicalutamide), of Tucker. Example 5 demonstrates that Bicalutamide is metabolically different from the claimed structures and is converted from exhibiting agonist to antagonist activity as a

function of metabolizing the compound, resulting in the oxidation of the thioether linkage to a sulfonyl linkage (see Perera et. al, *Drug metabolism and Disposition*, vol. 34(10), 1713-1721, 2006, attached hereto as Appendix 1).

In contrast, the metabolites of the SARM compounds represented by formulas I, II, III, IV, VII, VIII, IX, X possess an ether linkage and therefore oxidation does not occur at this labile site. Thus, the major metabolites in dogs of compound IV, for example is the nitro-reduced product and the deacetylated metabolite, while the major metabolite of compound III is the hydroxylated metabolite.

The only O-bridged compounds described in Tucker lack substituents of the phenolic ring, in marked contrast to those claimed in the subject Application. Applicants submit that the phenyl substituent is involved in specific hydrogen bonding with the androgen receptor ligand binding domain, which participates in the transcriptional activation activity of such compounds (see for example, C.E. Bohl et. al. in *J. Biol. Chem.* vol. 280, No. 45, p. 37747, 2005, attached hereto as Appendix 2).

It would not be obvious based on Tucker, to arrive to the claimed metabolites of the substituted O-bridged compounds since Tucker does not describe nor provide any foundation for the role of the phenyl-substituent and O-bridge moiety, which impart the unique characteristics to the claimed compound., as described above. Certainly Tucker provides no description nor foundation for metabolites of such compounds. Accordingly, Applicants request withdrawal of the rejection.

Miller does not describe nor provide any foundation for the claimed SARM metabolites. Specifically Miller describes radiolabelled SARMs only, and their use in imaging prostate cancer, alone, with only S-bridged compounds exemplified in this context. It would not be obvious, based on Miller, to obtain the claimed O-bridged SARM metabolites of this invention, as one skilled in the art would not be motivated to obtain unlabelled metabolites to image prostate cancer.

Neither Miller nor Tucker, alone or in combination indicate that the major metabolite of O-bridged SARM compounds are the hydroxylated metabolite (oxidation), the hydrolyzed metabolite, the deacetylated metabolite (for compound IV) or the aminated metabolite. Thus, the metabolites of Compounds I, II, III, IV, VII, VIII, IX, X are not obvious to one skilled in the art.

The Examiner alleged that administration of comparable compounds renders metabolites thereof inherent properties of the comparable compounds. Applicants disagree. Applicants are not aware of any case law that supports that assumption, and invite the Examiner to supply such case law to support his rejection. Applicants maintain that the Examiner's allegation that the compounds are comparable is erroneous. Neither Miller nor Tucker, alone or in combination, lead the skilled artisan to the specific SARM compounds of the formulas I, II, III, IV, VII, VIII, IX, X, which are unique in that they possess anabolic activity, whereas the compounds of Tucker do not possess such activity, therefore the compounds are not comparable. Moreover, Applicants have demonstrated that the metabolite profile for the compounds differs as a function, *inter alia,* of the bridging moiety. Thus, neither the compounds, nor the metabolite profile for such compounds is comparable. Certainly, neither Tucker nor Miller lead the skilled artisan to the hydroxylated, deacetylated, or aminated derivatives of the compounds of formulas I, II, III, IV, VII, VIII, IX, X, as claimed in the present invention. Accordingly, the metabolites are not obvious, and Applicants request withdrawal of the rejection.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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Dated: January 2, 2008

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